TRANSLATION

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

| Applicant's or agent's file reference | FOR FURTHER ACTION | See Form PCT/IPEA/416 |
|---|---|---|
| 85SL0511 | | |
| International application No. | International filing date *(day/month/year)* | Priority date *(day/month/year)* |
| PCT/EP2004/014310 | 15.12.2004 | 01.03.2004 |
| International Patent Classification (IPC) or national classification and IPC | | |
| C12Q1/68 | | |
| Applicant | | |
| SIRS-LAB GMBH | | |

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of _____ sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

   a. ☒ *(sent to the applicant and to the International Bureau)* a total of 5 sheets, as follows:

      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))

      _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

| | | |
|---|---|---|
| ☒ | Box No. I | Basis of the report |
| ☐ | Box No. II | Priority |
| ☒ | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| ☐ | Box No. IV | Lack of unity of invention |
| ☒ | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| ☐ | Box No. VI | Certain documents cited |
| ☐ | Box No. VII | Certain defects in the international application |
| ☐ | Box No. VIII | Certain observations on the international application |

| Date of submission of the demand | Date of completion of this report |
|---|---|
| Name and mailing address of the IPEA/EP<br><br>Facsimile No. | Authorized officer<br><br>Telephone No. |

**INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY**

International application No.
PCT/EP2004/014310

**Box No. I Basis of the report**

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (Rule 12.3 and 23.1(b))

☐ publication of the international application (Rule 12.4)

☐ international preliminary examination (Rule 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ the international application as originally filed/furnished

☒ the description:

pages 1-21,23-30 as originally filed/furnished

pages* 22 received by this Authority on 31.05.2006 with letter of 30.05.2006

pages* _____ received by this Authority on _____

☒ the claims:

nos. _____ as originally filed/furnished

nos.* _____ as amended (together with any statement) under Article 19

nos.* 1-23 received by this Authority on 31.05.2006 with letter of 30.05.2006

nos.* _____ received by this Authority on _____

☐ the drawings:

sheets _____ as originally filed/furnished

sheets* _____ received by this Authority on _____

sheets* _____ received by this Authority on _____

☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

**INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY**

International application No.
PCT/EP2004/014310

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 10,18,19 (in part)

because:

☐ the said international application, or the said claims Nos. _____
relate to the following subject matter which does not require an international preliminary examination (*specify*):

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 10,18,19 (in part)
are so unclear that no meaningful opinion could be formed (*specify*):

See supplemental sheet

☒ the claims, or said claims Nos. 10,18,19 (in part) are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. _____

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☒ See Supplemental Box for further details.

**Box No. V** **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Claims | 1-23 | YES |
| | Claims | | NO |
| Inventive step (IS) | Claims | 1-23 | YES |
| | Claims | | NO |
| Industrial applicability (IA) | Claims | 1-23 | YES |
| | Claims | | NO |

2. Citations and explanations (Rule 70.7)

## 1. CITATIONS

D1: US 2004/096917 (IVEY RICHARD M ET AL) 20 May 2004 (2004-05-20)

D2: WO 2004/087949 (SIRS-LAB GMBH) 14 October 2004 (2004-10-14)

D3: PRUCHA ET AL.: "Expression profiling: Toward an application in sepsis diagnostics", SHOCK, vol. 22, no. 1, July 2004 (2004-07), pages 29-33

D4: CHINNAIYAN ET AL.: "Molecular signatures of sepsis. Multiorgan gene expression profiles of systemic inflammation" AMERICAN JOURNAL OF PATHOLOGY, vol. 159, October 2001 (2001-10), pages 1199-1209

D5: PATHAN ET AL.: "The complexity of the inflammatory response to meningococcal sepsis revealed by gene expression profiling using cDNA microarrays" CRITICAL CARE MEDICINE, vol. 30, no. 12, December 2002 (2002-12), page A47

D6: WIEGAND ET AL.: "Gene expression pattern in human monocytes as a surrogate marker for

systemic inflammatory response syndrome (SIRS)" MOLECULAR MEDICINE, vol. 5, 1999, pages 192-202

## 2. NOVELTY (PCT Article 33(2))

2.1 The examination for novelty and inventive step was carried out in the absence of the priority document, with the provisional assumption of the application having a valid priority.

2.2 The application describes a method for *in vitro* distinction of systemic inflammatory noninfectious conditions (*i.e.* SIRS) and systemic inflammatory infectious conditions (*i.e.* sepsis), using gene expression patterns and quantification thereof, which make such a differentiation possible.

2.3 Such a method has not been described by any of documents D4-D6 at the time of application.

2.4 The application therefore meets the criteria of PCT Article 33(2) because the subject matter of amended claims 1-23 is novel with regard to the prior art, in agreement with the Regulations (PCT Rule 64(1) to (3)).

## 3. INVENTIVE STEP (PCT Article 33(3))

3.1 Any of documents D4-D6 can be considered the prior art closest to the subject matter of claim 1. Thus, for

example, D4 discloses the use of cDNA microarrays for determining gene expression patterns of 7398 genes relevant to sepsis (whole document). In contrast to the application, however, no expression patterns for SIRS are determined in D4. The same applies, conversely, also to D5 which discloses expression of SIRS-relevant genes but not of those that would be characteristic for sepsis (also whole document).

3.2 The difference between the application and each of D4-D6 is therefore simultaneous determination of SIRS-specific gene expression patterns and of sepsis-specific gene expression patterns in order to be able to distinguish between both pathologies. The problem addressed by the application therefore comprises the need for a method which makes such a distinction possible. The solution proposed by the application is to identify the specific genes specified in claim 1g) [see also tables 2 and 3 of the description] which are specifically overexpressed in SIRS or underexpressed in sepsis [compared to control genes and the respective other pathology].

3.3 It would be clear to a person skilled in the art that, by comparing gene expression patterns of SIRS-specific gene expression patterns to those representing sepsis-specific gene expression patterns, genes or gene fragments can be identified that would be suitable specifically for differentiating between the two pathologies. However, a person skilled in the art would not necessarily obtain, as a result, the 68 specifically identifed genes provided as solution in the application

but other, alternative sets of genes.

3.4 In addition, the prior art, by way of example of D4-D6, does also not reveal simultaneous determination of the expression patterns SIRS- and sepsis-specific gene expression patterns. Claim 1 therefore involves an inventive step under PCT Article 33(3).

3.5 The same also applies to dependent claims 2-23 for which, for said reasons, an inventive step can likewise be acknowledged.

3.6 The application therefore meets the criteria of PCT Article 33(3) because the subject matter of amended claims 1-23 is inventive with regard to the prior art, in agreement with the Regulations (PCT Rule 64(1) to (3)).

**INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY**

International application No.
PCT/EP2004/014310

**Supplemental Box Relating to Sequence Listing**

**Continuation of Box No. I, item 2:**

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:

   a. type of material

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing

   ☒ contained in the international application as filed

   ☒ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purposes of search and/or examination

   ☐ received by this Authority as an amendment* on _____

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

The sequence listing in the description, pages 1-114 as originally filed.

* *If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."*

**Supplemental Box**

In case **the space in any of the preceding boxes is not sufficient.**
Continuation of:

Box I:

I.1 Documents D1-D3, published between priority date and filing date, include (substantial) parts of the application as claimed. These documents are irrelevant with respect to novelty and inventive step under the current PCT procedure. However, if the applicant continues to pursue the EPC route, the following must be taken into account: depending on the result of examining the validity of the priority (*i.e.* should the priority of the application not be valid), D1-D3 may be cited against novelty and inventive step (for example together with D4-D6) of the (entire) set of claims.

Box III:

III.1 As stated in the international search report, claims 10 (in part) and also 18 and 19 (in part) lack the requisite support (PCT Article 5) and clarity (PCT Article 6). Neither the application nor the examples reveal the SEQ ID nos of those specified in tables 2 and 3 [with respect to claim 10] that might be suitable for distinguishing between SIRS and sepsis or identify the enzymatic or chemical RNA derivatives [with respect to claims 18 and 19].

III.2 Since the search was restricted to those parts of the claims that can be considered disclosed, clear and supported (PCT Article 5 and 6), *i.e.* the use of the SEQ

Supplemental Box

ID nos of tables 2 and 3, which are explicitly mentioned in (new) claim 1 and which appear to have proven suitability for differentiating between SIRS and sepsis, a correspondingly reduced expert opinion on novelty, inventive step and industrial applicability has been established.

III.3 (Parts of) claims 10, 18 and 19 which have not been searched are not examined for novelty, inventive step and industrial appliability.